Congressional Research Service

Memorandum November 17, 2003

TO: House Subcommittee on Criminal Justice, Drug Policy and Human Resources
Attention: Roland Foster

FROM: Judith A. Johnson
Specialist in Life Sciences
Domestic Social Policy Division

SUBJECT: **Human Papillomavirus**

In order to provide the information you requested on human papillomavirus (HPV), I contacted the following four organizations: the Centers for Disease Control and Prevention (CDC), the National Institutes of Health (NIH), the American College of Obstetricians and Gynecologists (ACOG), and the Partnership for Prevention. Copies of the responses I received from CDC and the Partnership for Prevention are attached; NIH replied that they do not have the type of information you are seeking (copy of email response is attached). ACOG has not yet responded. I also looked at reports on the Kaiser Family Foundation website on the topic of HPV and Sexually Transmitted Diseases prepared by Kaiser and the American Social Health Association. Copies of these reports are also attached. In response to your request, I am providing below a consolidation of the information obtained on HPV, primarily from CDC, on the overall size, cost, and impact of HPV in the United States. Most of the information was taken verbatim from CDC documents.

1. The overall prevalence and incidence of HPV in the United States.

According to information provided on the CDC website, an estimated 20 million Americans are currently infected with HPV (prevalence) and an estimated 5.5 million Americans become infected with HPV each year (incidence).[1] An estimated 75% of the reproductive age population has been infected with sexually transmitted HPV and an estimated 15% of Americans ages 15 to 49 are currently infected. A U.S. study published in 1998 found that an average of 14% of female college students became infected with genital HPV each year. About 43% of the women in the 1998 study were infected with HPV

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[1] All statistics in this Section 1 were found in the following document: *Tracking the Hidden Epidemics 2000 – Trends in STDs in the United States: A Closer Look at HPV Infection.* See: [http://www.cdc.gov/nchstp/od/news/RevBrochure1pdfcloselookhpv.htm].

during the 3-year study period. Although less data are available on HPV among men, levels of current infection in men appear to be similar to those in women.

HIV-positive individuals have a higher prevalence of HPV infection and precancerous lesions on the cervix and anus than HIV-negative individuals. A San Francisco study of gay and bisexual men found that 60% of HIV-negative men had HPV and almost all HIV-positive men with severely compromised immune systems were infected with HPV. Similarly, a six-city study among high risk and HIV-infected women found that 26% of HIV-negative women were infected with HPV but 70% of HIV-positive women with severely comprised immune systems were infected with HPV.

2. A detailed description of all HPV-related medical conditions and how each is treated.

Of the more than 100 HPV viruses that have been identified, about 30 can infect the genital area and are spread (almost always) through sexual contact.[2] Some are considered "high-risk" types and may cause abnormal Pap smears and cancer of the cervix, anus, and penis. Others are "low-risk," and they may cause mild Pap smear abnormalities and genital warts. However, most HPV infections are subclinical: they have no signs or symptoms. Therefore, most infected persons are completely unaware they are infected and can transmit the virus to a sex partner. Genital warts are extremely common and can appear within several weeks, several months or even years after sexual contact with an infected person. Therefore, it is often difficult for patients to determine when they became infected and which sexual partner was the source of the infection.

Visible genital warts can be removed, but no treatment is better than another and no single treatment is ideal for all cases. In most patients treatment can induce wart-free periods. If left untreated, visible genital warts may resolve on their own, remain unchanged, or increase in size or number. Determining whether treatment of genital warts will reduce transmission is difficult because laboratory markers of infectivity have not been established and because some clinical studies have found HPV DNA in genital tissue following treatment. Currently available therapies for genital warts may reduce, but probably do not eradicate, infectivity. Whether the reduction in viral DNA that results from current treatment regimens impacts future transmission remains unclear. The natural history of genital warts is generally benign; the types of HPV that usually cause external genital warts are not associated with cancer. No evidence indicates that either the presence of genital warts or their treatment is associated with the development of cervical cancer.[3] Recurrence of genital warts within the first several months after treatment is common and usually indicates recurrence rather than reinfection.

Treatment of external genital warts can either be administered in the doctor's office (cryotherapy, surgical removal, electrocautery, laser surgery, podophyllin resin, trichloroacetic acid, bichloroacetic acid, interferon injection) or applied at home by the

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[2] Genital HPV Infection. See: [http://www.cdc.gov/nchstp/dstd/Fact_Sheets/FactsHPV.htm].

[3] Visible genital warts usually are caused by HPV types 6 or 11. Other HPV types that cause flat, nearly invisible abnormal growths (as compared with types 6 and 11) in the anogenital region (e.g., types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, and 69) have been strongly associated with cancer in both men and women. See: [http://cis.nci.nih.gov/fact/3_20.htm].

patient (podofilox cream, imiquimod cream). Treatment of internal genital warts (cervix, vagina, urinary tract, anus, rectum, mouth) usually occurs in the doctor's office.[4]

Subclinical HPV infection is even more common than genital warts and there is currently no treatment available. Most HPV infections appear to be temporary and are probably cleared up by the body's immune system. One 1998 study in college students showed that in 91% of women with new HPV infections, HPV became undetectable within 2 years.[5] However, reactivation or reinfection with HPV is always possible.

The single most important risk factor for cervical cancer–regardless of whether warts are present or not–is persistent cervical infection with certain types of HPV. HPV type 16 accounts for more than 50% of cervical cancers and high-grade dysplasia (abnormal cell growth), and HPV 16 along with types 18, 31, and 45 account for about 80% of cervical cancers.[6] Regular screening with a cervical Pap test is an effective low cost screening test for the prevention of invasive cervical cancer.[7] Cervical cancer is treated using surgery, radiation and chemotherapy; sometimes two or more methods are used. The most common types of surgery include cryosurgery, laser surgery, cone biopsy, simple hysterectomy, radical hysterectomy and pelvic lymph node dissection, and pelvic exenteration (radical hysterectomy and bladder, vagina, rectum, and part of colon may be removed as well). Radiation therapy may involve external radiation or internal radiation (radioactive materials implanted in the tumor). Chemotherapy uses drugs to stop the growth of cancer cells, either by killing the cells or by stopping the cells from dividing. When taken by mouth or injected into a vein or muscle, the drugs enter the bloodstream and can reach cancer cells throughout the body. The type and stage of the cervical cancer being treated determines which chemotherapy drug is used and the method of administration.[8]

Cervical dysplasia is a premalignant or precancerous change in the cells of the cervix which may progress to cancer without treatment. Mild dysplasia (also called low-grade squamous intraepithelial lesions or low-grade SILs) is a common condition, especially in young women, and a majority of cases return to normal over several months to a few years. Sometimes, mild dysplasia can progress to moderate or severe dysplasia, also called high-grade SILs. High-grade SILs are not cancer, but they may eventually lead to cancer and are treated by a doctor when they are detected. Treatments for cervical dysplasia include surgery, cone biopsy, cryosurgery, laser surgery, and electrosurgery.[9]

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[4] For more detailed information, see: *Sexually Transmitted Diseases Treatment Guidelines 2002-Human Papillomavirus Infection* at [http://www.cdc.gov/std/treatment/6-2002TG.htm]

[5] The polymerase chain reaction (PCR) and another technique (Southern blot hybridization) were used to detect HPV in cell samples from the cervix and vagina. Gloria Y. F. Ho, et al., Natural History of Cervicovaginal Papillomavirus Infection in Young Women, *The New England Journal of Medicine*, vol. 338, Feb. 12, 1998, pp. 423-428.

[6] Ibid.

[7] For more detailed information, see: *Cervical Cancer and Pap Test Information* at [http://www.cdc.gov/cancer/nbccedp/info-cc.htm]

[8] More detailed information on cervical cancer treatment can be found at [http://www.nci.nih.gov/cancerinfo/pdq/treatment/cervical/patient/] for patients, and [http://www.nci.nih.gov/cancerinfo/pdq/treatment/cervical/healthprofessional] for physicians.

[9] Guidelines for the treatment of cervical dysplasia can be found at :

(continued...)

3. The overall annual cost for testing and treatment of HPV-related medical conditions.

In the United States, HPV is associated with about 80% of the 12,000 cases and 4,100 deaths due to cervical cancer each year.[10] HPV is also associated with more than one million precancerous lesions of varying severity. The direct medical cost of treating a patient with cervical cancer is $9,200 to $13,360, while surgery to remove a precancerous lesion is $1,100 to $4,360.[11] The financial burden of HPV in the U.S. has been estimated to be from $1.6 billion to $6 billion annually, making HPV one of the most costly sexually transmitted diseases (STDs) after HIV infection.[12]

4. The annual number of HPV-related diagnoses requiring invasive medical procedures.

Almost all of the invasive medical procedures for HPV are linked to cervical cancer. In the United States, HPVs are associated with about 80% of the 12,000 cases and 4,100 deaths due to cervical cancer each year. They are also associated with more than one million precancerous lesions of varying severity.[13]

5. A ranking of all sexually transmitted diseases, including HPV, in order by: cost for testing and treatment; prevalence; and, associated deaths, including HPV-related cervical cancer deaths.

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[9] (...continued)
[http://www.guidelines.gov/summary/summary.aspx?doc_id=3286&nbr=2512&string=cervical+AND+cancer].

[10] A. Jemel et al., Cancer Statistics, 2003, *CA – A Cancer Journal for Clinicians*, vol. 53, Jan./Feb. 2003.

[11] Preventing Emerging Infectious Diseases: A Strategy for the 21st Century, Box 2: Economic Costs for Patient Care from Infectious Diseases, United States visited at [www.cdc.gov/ncidod/emergplan/box02.htm]. Also, an article in the January 2003 issue of *Emerging Infectious Disease* examined the cost-effectiveness of an HPV vaccine and calculated many of the resultant costs of screening and treatment. See attached and online at: [http://www.cdc.gov/ncidod/EID/vol9no1/02-0168.htm].

[12] CDC, Prevention of Genital HPV Infection and Sequelae: Report of an External Consultants' Meeting, Atlanta, GA: CDC, National Center for HIV, STD and TB Prevention; Dec. 1999.

[13] See Box 2, p. 2 in: CDC. Preventing Emerging Infectious Diseases: A Strategy for the 21st Century, at [http://www.cdc.gov/ncidod/emergplan/box02.htm]; and Cancer Statistics, 2003.

Table 1. Cost of Sexually Transmitted Diseases, 1994

STD	Cost (in millions)
Sexually transmitted HIV	$4,683
Pelvic Inflammatory disease	4,148
HPV	3,827
Chlamydia	2,013
Gonorrhea	1,051
Cervical cancer	737
Herpes simplex	237
Hepatitis B	156
Syphilis	106
Chancroid	1

Source: Institute of Medicine, The Hidden Epidemic: Confronting Sexually Transmitted Diseases, 1997.

Table 2. Prevalence of Sexually Transmitted Diseases

STD	Prevalence
Herpes	45,000,000
HPV	20,000,000
Chlamydia	2,000,000
Hepatitis B	417,000
Gonorrhea	n/a
Syphilis	n/a
Trichomoniasis	n/a
Bacterial vaginosis	n/a

Source: Tracking the Hidden Epidemics 2000 – Trends in STDs in the United States. [http://www.cdc.gov/nchstp/dstd/Stats_Trends/Trends2000.pdf]

According to CDC, there has not been a recent study summarizing in a comparable manner all deaths from STDs. In 2002, there were approximately 9, 000 AIDS deaths among those who were infected through sexual transmission of HIV. Other deaths due to AIDS that year were associated with other sources of transmission.[14] **Table 3** below provides data from 1992 regarding deaths among women.

[14] The most current HIV/AIDS surveillance report with these data can be found at: [http://www.cdc.gov/hiv/stats/hasrlink.HTM].

Table 3. Mortality Related to Sexually Transmitted Diseases in U.S. Women, 1992

STD	Deaths
Cervical cancer	5,210
HIV	2,665
Hepatitis B and Hepatitis C	960
Syphilis	99
Pelvic inflammatory disease	220
Ectopic pregnancy	18
Gonorrhea	43
Other	4
Total	**9,179**

Source: American Journal of Public Health, vol. 87(6), June 1997, pp. 938-944.

6. A description of all HPV specific prevention and education programs supported by the Centers for Disease Control and Prevention or other federal agencies.

CDC provided me with a copy of a August 2003 Report to Congress entitled "Human Papillomavirus: Surveillance and Prevention Research," which was prepared by CDC in response to the Public Health Service Act Section 317P. This report describes activities undertaken to date to address the requirements of that section. However, there are additional programs at CDC that address cervical cancer.

I trust this information will be useful to your office. If you have any further questions, please do not hesitate to call (202-707-7077).

Attachment